MARKED UP VERSION OF AMENDED CLAIMS

22. (Twice Amended) A tablet [solid pharmaceutical dosage form] adapted for direct oral administration across the oral mucosa comprising:

a pharmaceutically effective amount of a [an orally-administrable] medicament capable of buccal, sublingual and gingival administration; and

at least one saliva activated effervescent [agent] couple present in an amount which is greater than the amount necessary for tablet disintegration and which is sufficient to increase either the rate of the extent of absorption of said medicament across the oral mucosa, and wherein said amount of said at least one effervescent couple is between about 5% by weight and about 80% by weight.

23. (Amended) The tablet [solid pharmaceutical dosage form] of claim 22, wherein said effervescent couple [agent] is present in an amount between about 20% by weight and about 80% by weight.

24. (Amended) The tablet [solid pharmaceutical dosage form] of claim 22, further comprising at least one pH adjusting substance.

25. (Amended) The tablet [solid pharmaceutical dosage form] of claim 22, further comprising a bioadhesive, wherein said bioadhesive increases the contact time between said tablet [dosage form] and the oral mucosa.

26. (Amended) The tablet [solid pharmaceutical dosage form] of claim 22, further comprising a non-effervescent disintegration agent.

27. (Amended) The tablet [solid pharmaceutical dosage form] of claim 22, further comprising glidants, lubricants, binders, sweeteners, flavoring and coloring components.

28. (Amended) The tablet [solid pharmaceutical dosage form] of claim 22, wherein said [orally administerable] medicament is selected from the group consisting of analgesics, anti-inflammatories, antipyretics, antibiotics, antimicrobials, laxatives, anorexics, antihistamines, antiasthmatics, antidiuretics, antiflatuents, anti-emetics, antimigraine agents, antispasmodics, sedatives, antihypertensives, tranquilizers, decongestants, and beta blockers.

29. (Amended) The tablet [solid pharmaceutical dosage form] of claim 22, wherein said [orally administerable] medicament is selected from the group consisting of peptides, proteins and oligonucleotides.

30. (Amended) A tablet [solid pharmaceutical dosage form] adapted for direct oral administration across the oral mucosa comprising:

a) a pharmaceutically effective amount of an orally administerable medicament capable of existing in an ionized form and a unionized form in the mouth;

b) at least one saliva activated effervescent [agent] couple present in an amount [sufficient to increase absorption of said orally administerable medicament across the oral mucosa] which is greater than the amount necessary for tablet disintegration and which is sufficient to increase either the rate of the extent of absorption of said medicament across the oral mucosa; and

c) at least one pH-adjusting substance present in an amount which is sufficient to change the pH of a local environment of said dosage form at a site of absorption in the mouth to favor said unionized form of said medicament

[one or more glidants, lubricants, binders, sweeteners, flavoring, non-effervescent disintegration agents or coloring components].

31. (Amended) The [solid pharmaceutical dosage form] tablet of claim 30, further comprising at least one [pH adjusting substance] glidant, lubricant, binder, sweetener, flavor, non-effervescent disintegration agent or color.

33. (Amended) The [solid pharmaceutical dosage form] tablet of claim 30, comprising a non-effervescent disintegration agent selected from the group consisting of microcrystalline cellulose, croscarmellose [croscarmelose] sodium, crospovidone, corn starch, potato starch, modified corn starch, modified potato starch, bentonite, alginates, agar, guar, locust bean, karaya, pecitin and tragacanth..

36. (Amended) The [solid pharmaceutical dosage form] tablet of claim 30, wherein said at least one saliva activated effervescent [agent] couple is present in an amount between about 20% by weight and 80% by weight.

REMARKS

Entry of the foregoing and reexamination and reconsideration of the above-captioned application, as amended hereby, pursuant to and consistent with 37 C.F.R. § 1.112, and in light of the remarks that follow are respectfully requested.

On June 27, 2002, the undersigned submitted an amendment pursuant to 37 C.F.R. § 1.116. The amendment was not entered as it allegedly raised new issues and raised issues of new matter. Applicants again proffer those amendments, as well as others, and disagree that new issues or issues of new matter are raised. In the previous final action, claim 22 and the claims dependent therefrom were rejected pursuant to 35 U.S.C. § 102 over DiSanto. To the extent that that rejection would be applied to the claims as amended, applicants respectfully traverse. The examiner has argued that the amount of sodium bicarbonate recited in example 3 in DiSanto is 61% and accordingly DiSanto reports an amount of effervescent material falling within the range of 5-80% as claimed in claim 22.

As noted in applicants' prior amendment after final rejection, claim 22 refers to an effervescent "agent." However, as the definition makes clear, this "agent" is synonymous with "couple." As explained at page 5 of the specification, the term "effervescent agent" includes compounds that evolve gas. The preferred effervescent agents evolve gas by means of a chemical reaction that takes place upon exposure of the effervescent agent (an effervescent couple) to water and/or to saliva in the mouth. Since the term "effervescent couple" appears in the specification as filed, the addition of that term to the claims does not raise issues of new matter.

Applicants respectfully submit that it is inconsistent with both applicants' definition and the common usage of the term "effervescence" to consider only the weight percentage of one of the ingredients of the effervescent couple without also considering the other. In this case, it would be improper to consider merely the percentage of sodium bicarbonate present without, at the very least, also considering the amount of citric acid recited in example 3. If citric acid is also considered, then the amount of effervescent material, the amount of effervescent couple, is well over 80% of the tablet weight. Accordingly, DiSanto cannot anticipate the claims, as it discloses the use of an effervescent couple in an amount outside of the claimed range. While applicants believe that the terms "agent" and "couple" are, in this context, identical in scope, the amendment is offered to clarify the situation and to address the examiner's concern.

The claims were also previously rejected as obvious. However, as that rejection would be applied to the claims as amended, applicants again traverse. If DiSanto does not anticipate the claimed invention, which it cannot, it cannot possibly render the claims obvious. DiSanto provides nothing more than a single example, with essentially no explanation, of a particular effervescent formulation for one drug. It provides no discussions of modifying the formulation in any way.

There is nothing in DiSanto to teach, suggest or motivate one of ordinary skill in the art to modify the amount of effervescent couple recited in example 3. Indeed, applicants have been unable to find another reference to effervescence anywhere in the specification. Nothing in the DiSanto reference teaches or suggests that the amount of effervescents used can be important for purposes of transporting material across the mucosal membrane in the mouth or that particular amounts of material are preferred for this purpose.

In short, other than a solitary serendipitous disclosure of a formulation with little or no explanation, DiSanto is not a relevant teaching or suggestion of anything broader at all. One of ordinary skill in the art could not look to example 3 of DiSanto and, based upon its teaching or any of the other teachings of the DiSanto reference, arrive at the present invention. DiSanto does not suggest the goal of improving absorption to the use of effervescents or even suggest a manner in which it can be achieved. It certainly does not describe what criteria are necessary in a tablet for achieving this purpose. And the secondary reference in no way addresses these deficiencies. Based on this difference alone, applicants respectfully submit that the claims as amended are both novel and unobvious over DiSanto.

To further accentuate the differences between the present invention and the prior art, applicants have amended claim 22 to make it clear that in the invention, a saliva activated effervescent couple is present in an amount that is greater than the amount necessary for tablet disintegration. Indeed, the amount of saliva activated effervescent disintegration couple present must be sufficient to increase either the rate or the extent of absorption of the medication across the oral mucosa. Applicants have found that effervescents can be used for far more than merely allowing for disintegration of the tablet. While rapid disintegration exposes the drug such that it may be used by the body, unless an effervescent couple is present in sufficient amounts, amounts greater than that necessary for disintegration, it does not significantly participate in the drug absorption process. By providing effervescents in an amount that is greater than that necessary

for achieving disintegration of the dosage form, it is possible to obtain these benefits. Nothing in DiSanto teaches or suggests the need for such additional amounts of effervescent agent.

Claim 30 has also been amended to require that the drug used be capable of existing in either an ionized or an unionized form in the mouth. The claim also requires a saliva activated effervescent couple and at least one pH adjusting substance. The pH adjusting substance must be present in an amount that is sufficient to change the pH of the local environment of the tablet at a site of absorption in the mouth in such a way that it will favor the unionized form of the particular medicament. Whether this pH adjusting substance will raise or lower the pH will depend on the medicament in question. Nothing in the DiSanto reference teaches or suggests this concept nor the presence of both an effervescent couple and a separate pH adjusting substance. The secondary reference cited by the examiner in a prior action does not address these issues either.

For all of the foregoing reasons, applicants believe that the claims as amended are novel and unobvious and respectfully request a withdrawal of the prior rejections. Should the examiner have any questions with regard to the foregoing, the examiner should contact the undersigned, at the examiner's convenience, at 908 654 5000. Furthermore, should any fee be due and owing in this regard, the examiner is authorized to charge deposit account no. 12-1095 therefor.

From the foregoing, further and favorable action in the form of a notice of allowance is believed to be next in order and such action is earnestly solicited.

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Respectfully submitted,

By_____

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